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REMARKS

The claims have been amended to delete the term "transformant" to which the Examiner objected. The term has been replaced by the term "substrate" which appears at page 6, lines 16-17 of the specification.

Applicants respectfully submit that the term "transformant" was supported in the specification at page 1, lines 9-15, page 2, lines 5-9. The term "transformant" as set forth in the specification refers to the compound which is transformed by the microorganisms into the desired useful product. However, the amendment to the claims obviates the Examiner's rejection.

Applicants respectfully request that the Examiner reconsider the requirement for restriction. The requirement was discussed in great detail in the previous amendments. However, Applicants submit that the application was filed under 35 USC 371 and meets the unity of invention requirements set forth by the PCT. Applicants therefore respectfully submit that the requirement for restriction be reconsidered and withdrawn.

As presently claimed, the invention is directed to a reaction medium for fermentation processes comprising (a) microorganisms; (b) a phase inversion temperature emulsion, wherein the emulsion comprises water, an emulsifier and an oil phase selected from the group consisting of (i) fatty acid alkyl esters, vegetable triglycerides and mixtures thereof comprising a carbon source or a substrate.

Claims 12-22 stand rejected under 35 USC 103(a) as unpatentable over Inlow et al. (U.S. 5,372,943) in view of Kopp-Holtwiesche (DE 3738812; hereinafter DE) and Forster

et al. (WO 95/11660; hereinafter WO). Applicants respectfully submit that Inlow et al., DE and WO whether considered alone or in combination neither teach nor suggest the present invention.

Applicants respectfully request that the Examiner reconsider the teachings of Inlow et al. Inlow et al. is directed to a microemulsion containing small amounts of micro nutrients which facilitate the growth of the microorganisms. However, Applicants respectfully submit that the microemulsions disclosed in Inlow et al. do not contain a sufficient amount of any material which would permit the microemulsion to be a source of carbon or a substrate which is transformed in the culture medium. It is clear from Table 1 that the culture medium contains major amounts of a carbon source and only micro amounts of a micronutrient provided by the microemulsion.

Applicants invite the Examiner's attention to the examples in the present application which show the relatively large amounts of the fatty acid esters present in the microemulsion. The microemulsion can be utilized as the sole carbon source for the fermentation process.

In contrast to the present invention, Inlow et al. would teach one skilled in the art that the microemulsion could not be useful as the carbon source or as the substrate. If a sufficient amount of the Inlow et al. microemulsion were added to a fermentation system in amounts sufficient to provide a carbon source or a substrate, the culture medium would be so diluted that it would not be possible or useful to attempt to recover a valuable product from the extremely dilute composition. As shown in Table 1, the carbon source in the Inlow

et al. process are the various unfiltered peptones and soluble ingredients. The materials are present in substantial amounts and provide the carbon source for the culture medium.

The microemulsion of Inlow et al., as shown in Table 1, is present in such a small amount that the lipids could not be useful as a carbon source or a substrate without extreme dilution of the culture medium with the impossibility or the difficulty in attempting to recover any converted materials which would be present in such small amounts as micrograms per liter.

The deficiencies in Inlow et al. are not cured by DE. DE is directed to a *candida tropicalis* strain which has been modified to a strain which converts methyl laurate to the corresponding alpha-omega dicarboxylic acid methyl ester. As shown in the examples, the fatty acid ester is present in the fermentation medium in large amounts along with a separate carbon source. Example 1 shows a culture medium containing 4% of methyl laurate and 2% of glucose. Example 2 discloses a fermentation medium containing 3% glucose (carbon source) and 2% methyl laurate (transformant). Example 3 shows compositions containing large amounts of the methyl ester (15 g/l).

DE is silent concerning introducing the methyl esters into the fermentation medium as a microemulsion. However, there is neither teaching nor suggestion that the material be introduced into the fermentation medium as a microemulsion or PIT emulsion of micro nutrients. Clearly, the methyl ester in DE is useful as the substrate or transformant. Applicants therefore respectfully submit that DE does not cure the deficiencies in Inlow et al.

The deficiencies in the combination of Inlow et al. with DE are not cured by combination with WO. WO is directed to a cosmetic composition which can be a microemulsion. However, there is neither teaching nor suggestion that the cosmetic composition of WO be added to a culture medium as a source of carbon or as a substrate or transformant. The Examiner has done some wild speculation to arrive at the conclusion that one skilled in the art would expect that the cosmetic preparation of WO would be a fermentation medium as understood in the present application. Applicants respectfully submit that one skilled in the art would not attempt to use the cosmetic formulations of WO as a fermentation medium and the constituents as a carbon source or a substrate or a transformant in the culture medium. The amounts of the components of the cosmetic formulation are present in the formulation in amounts much higher than in the microemulsion of the present invention. Applicants therefore respectfully submit that the Examiner is utilizing hindsight reconstruction of Applicants' invention to include the WO reference in a rejection. Clearly, one skilled in the art would not view a cosmetic preparation as a fermentation medium.

Applicants make this statement on the basis that one skilled in the art knows that cosmetic formulations generally contain agents which prevent fermentation of the cosmetic formulation and provide long term stability so that the cosmetic preparations can be formulated and sold over an extended period of time without spoiling due to mold, bacteria, yeast and the like.

Applicants therefore respectfully submit that the combination of WO with Inlow et al.

and DE is improper and Applicants respectfully submit that a rejection based on the combination of Inlow et al. with DE and WO is untenable and respectfully request that the rejection be reconsidered and withdrawn.

Inlow et al. is directed to a culture medium for use in culturing cells which produce a protein which has some use or activity. DE is directed to a culture medium for transforming a lauric acid methyl ester to an ester of dodecandioic acid. Applicants respectfully submit that there is no teaching nor suggestion that adding the large amounts of the fatty acid esters to the microemulsion would provide a useful medium for preparing the expressed proteins of the Inlow et al. reference. Applicants submit that it is clear that Inlow et al. process requires micro quantities of the fatty components in the microemulsion to increase the growth rate of cell culture. Fatty acid microemulsion is not utilized as a carbon source or as a substrate in the medium.

Deficiencies in the combination of Inlow et al. with DE are not cured by combination with WO. WO is directed to cosmetic preparation which is an aqueous emulsion formed by the PIT method. The cosmetic emulsion of WO contains a cosmetic active agent selected from the group consisting of deodorizing agents, perfume oils and light-protective factors (see Abstract). Applicants submit that there is no suggestion to include the cosmetic microemulsions of WO in the culture medium of Inlow et al. or DE.

As one skilled in the art of fermentation processes knows, the microorganisms to be cultured are very sensitive to the environment. This is particularly shown in Inlow et al. where the micro quantities of the microemulsion introduced into the culture medium

substantially increases the rate of cell growth. Also, it is well known in the art that many substances have an adverse effect on the growth of microorganisms in a culture medium. Applicants submit there is no suggestion that the addition of the cosmetic microemulsion disclosed in WO would be suitable for introduction to a culture medium as a carbon source or a substrate. Applicants respectfully submit that there is no teaching nor suggestion that the addition of the cosmetic microemulsion into the culture medium in Inlow et al. at a concentration much higher than that disclosed in Inlow et al. would lead to a useful culture medium, or that a carbon source such as sugar could be replaced by the fatty acid esters or fatty acid triglycerides of vegetable origin. Applicants respectfully submit that the combination of Inlow et al. with DE and WO does not provide a prima facie case of obviousness of the invention. Applicants submit that the rejection is based on hindsight reconstruction of Applicants' invention.

As pointed out above, WO does not disclose a culture medium. Cosmetic formulations generally contain an ingredient which suppress or eliminates the growth of microorganisms which can attack the formulation. The cosmetic formulations are generally prepared for substantial shelf life and cannot tolerate fermentation which the Examiner proposes. Applicants again submit that the rejection is based on hindsight reconstruction of Applicants' invention and should be reconsidered and withdrawn.

Since Inlow et al. utilizes micro amounts of the microemulsion to increase the rate of proliferation of cells by supplying micro nutrients to the culture medium, coupled with DE which is directed to the use of major amounts of lauric acid methyl esters to produce

dodecandioic acid, Applicants respectfully submit there is neither teaching nor suggestion to introduce the lauric acid esters into the culture medium of Inlow et al. at the low concentration required in Inlow et al. to transform the lauric acid methyl esters into methyl esters of dodecandioic acid.

Applicants respectfully submit that as discussed above, Inlow et al. utilizes micro amounts of the fatty acid emulsion as a growth stimulant for the cells of the culture. DE utilized gross amounts of the lauric acid methyl ester as a transformant or substrate for the production of methyl ester of dodecandioic acid. Applicants respectfully submit that there is neither teaching nor suggestion to introduce large quantities of lauric acid methyl ester into the culture medium disclosed in Inlow et al. Applicants therefore respectfully submit that the references are not combinable and a rejection based therein is untenable.

As discussed above, WO is directed to cosmetic preparations formed by the PIT method. However, there is neither teaching nor suggestion that the cosmetic ingredients contained in the cosmetic preparation would provide a culture medium which is friendly to the propagation of desired microorganisms of Inlow et al. The Inlow et al. culture medium is designed to provide for active growth of the microorganism and extraneous ingredients are not introduced in the culture medium unless they are known to have a positive effect on the growth of the microorganism. Applicants submit that the microorganism of WO with the cosmetic ingredients could not teach nor suggest that the microemulsion could be introduced in a culture medium without an adverse effect on growth of the microorganism.

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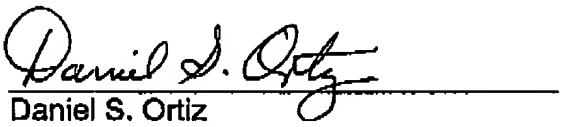
In view of the amendments entered in the claims and the above discussion, Applicants respectfully submit that the application is in condition for allowance and favorable consideration is requested.

Respectfully submitted,



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